

REMARKS/ARGUMENT

Claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 51, 53, 55-58, 60-75, 78-79, 84, 86, 88-89, 91-93, 95-96, and 98-120 were pending following Applicants' Amendment and Response filed on July 20, 2009.

In this paper, claims 1, 3-4, 8, 31-32, 37-39, 41-42, 53, 55-58, 66, 86, 88-89, and 91-92 are amended without prejudice or disclaimer. No new claims are added. Claims 51, 60-65, 67-75, 78-79, 84, 93, and 115-120 are canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter removed or canceled by amendment in future applications. With the entry of this amendment, claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 53, 55-58, 66, 86, 88-89, 91-92, 95-96, and 98-114 are pending in this application.

Independent claims 1, 39, 42 are amended to incorporate all the steps previously presented in claim 93, which is now canceled. In particular, claims 1, 39, and 42 are amended to include a step of concentrating a complex using a concentration channel in a microfluidic device, the concentration channel having at least one microscale dimension of between about 0.1 and about 500 microns. Support for this amendment is found in at least original claim 93 and paragraphs [0216]-[0218] of the specification. Performance of this step in the presence of a second polyanion is supported at least by paragraphs [0191]-[0195] of the specification. Also, to the extent a claim refers to a sandwich assay format or a competitive assay format, support for including a concentrating step is at least found in paragraphs [0205]-[0207] or [0208]-[0210], respectively.

The separating step that was previously presented in independent claims 1, 39, and 42 is modified by amendment to recite electrophoretically separating in the presence of a third polyanion a complex using a separation channel in a microfluidic device, the separation channel

having at least one microscale dimension of between about 0.1 and about 500 microns. Support for this amendment is found at least in original claims 1, 39, and 42 and paragraphs [0114]-[0115]. Support for conducting the separation in the presence of a third polyanion is found at least in paragraphs [0051]-[0060], and original claims 39 and 42.

Independent claims 1, 39, and 42, and dependent claim 42 are amended to modify the form of the recitation regarding the presence of a first polyanion during the contacting step. Support for the use of such charged polymers is found at least in paragraphs [0056]-[0057] and [0194]-[0195] of the specification. The recitation is modified only for clarity and consistency. Applicants do not believe that the prior form of the recitation was the basis for any rejection, or that as amended (“in the presence of a first polyanion”), the form by which the element is recited could serve as the basis of a rejection based on the art of record.

Independent claims 1, 39, and 42 are also amended to recite that polyanions associated with the concentrating step reduce interference with the respective methods for detecting or determining the complex. Note that although the term “third” is added by amendment to the claims, the “third polyanion” refers to the polyanion associated with the separating step, which was already recited in the claims. Support for reduced interference by a [second] polyanion associated with the concentrating step is found at least in paragraph [0192].

Claims 3, 4, and 8 are also amended to include the independent selection of a polyanion associated with the concentrating step. Support for these amendments are found at least at paragraph [0192], in conjunction with paragraphs [0053]-[0054] (“In the concentration method . . . the above-described charged polymer may also be used.”), as well as original claims 78-79, and 84.

To maintain consistency with the amendments to claim 1, claims 31 and 32 are amended to specify that the polyanion associated with the separating step is the “third polyanion.” Claims 37, 38, and 41 are amended to remove redundant language. Claim 91 is amended to correctly refer to the “first” polyanion and to recite language (“present” rather than “added to the sample buffer”) that has a proper antecedent basis. Basis for these amendments is found in the original claims, particularly original claim 90, which had been canceled previously. The amendments to claims 57-58, to recite “and,” are presented for clarity and consistency. Claims 53, 55-58, 66, 86, 88-89, and 91-92 are amended to update the claim dependency in view of the other amendments.

All of the above amendments either are supported by the specification and/or the original claims or are of a minor clerical nature. Accordingly, the amendments add no new matter. Applicants respectfully request reconsideration of the pending claims in the application.

I. General Remarks on Last Office Action

Applicants gratefully acknowledge that in the last Office Action, the Office withdrew the rejections of the claims made under Section 112, second paragraph, as being moot in view of the amendments.

In the last Office Action, the Office also, however, rejected the pending claims under Section 103, as allegedly being obvious over various combinations of the following references: WO 02/082083 to Kawabata et al. (“Kawabata”), U.S. Patent 5,611,903 to Janssens et al. (“Janssens”), Kaniansky et al. in Analytical Chemistry, Vol. 72, p. 3596 (2000) (“Kaniansky”), Brown et al. in J. Biol. Chem., Vol. 269, p. 26801 (1994) (“Brown”), U.S. Patent 5,571,680 to Chen et al. (“Chen”), U.S. Patent Application 2002/0079223 to Williams et al. (“Williams”), EP

1061370 A2 to Hosokawa et al. (“Hosokawa”), and Xu et al. in L. Leukocyte Biology, Vol. 72, p. 410 (2002) (“Xu”).

In brief, claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 51, 60-65, 68-70, 72-75, 78-79, 84, 86, 88-89, 91-92, 95, 101-102, 105-106, and 115-116 were rejected over Kawabata, in view of Janssens;

claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, 91-92, 101-112, and 115-118 were rejected over Chen, in view of Xu and Janssens;

claims 53, 55-58 were rejected over both (a) Kawabata, in view of Janssens, further in view of Kaniansky, and (b) Chen, in view of Xu and Janssens, further in view of Kaniansky;

claim 66 was rejected over both (a) Kawabata, in view of Janssens, further in view of Brown, and (b) Chen, in view of Xu and Janssens, further in view of Brown;

claims 93, 119, and 120 were rejected over Chen, in view of Xu and Janssens, further in view of Kaniansky, further in view of Williams;

claims 95-96, and 98-99 were rejected over Chen, in view of Xu and Janssens, further in view of Kawabata;

claims 42 and 113-114 were rejected over Hosokawa, in view of Xu and Janssens; and

claim 100 was rejected over Hosokawa, in view of Xu and Janssens, further in view of Kawabata.

By this amendment, Applicants present a claim set having three independent claims, claims 1, 39, and 42, all of which incorporate the limitations previously presented in claim 93. Claims 1, 39, and 42 are amended to include *inter alia* three steps that recite, in general terms, (a) contacting in the presence of a first polyanion a sample and a reagent/reagents, *e.g.*, an affinity molecule/charged carrier conjugate, (b) concentrating in the presence of a second

polyanion a complex/complexes that forms using a concentration channel, and (c) separating in the presence of a third polyanion a complex/complexes that forms using a separation channel.

As is discussed in greater detail below, Applicants note that, to reject independent claim 93 (and claims 119 and 120, which depended therefrom), which is the only independent claim previously presented that recited the three steps of contacting, concentrating, and separating, the Office applied five references, namely, Chen, in view of Xu and Janssens, further in view of Kaniansky, further in view of Williams. Because all pending claims now incorporate these limitations, Applicants submit that (a) the prior rejections applied to all claims other than claims 93, 119, and 120 are rendered insufficient, and (b) by overcoming the rejection applied to claim 93 based on these five references, the claims as amended herein should be allowed.

II. Claim Rejections Under 35 U.S.C. § 103 - Obviousness

A. Office Action, Section 7 at page 3: Claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 51, 60-65, 68-70, 72-75, 78-79, 84, 86, 88-89, 91-92, 95, 101-102, 105-106, and 115-116

Claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 51, 60-65, 68-70, 72-75, 78-79, 84, 86, 88-89, 91-92, 95, 101-102, 105-106, and 115-116 (but not claim 93) were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata, in view of Janssens.

Applicants respectfully traverse these rejections in view of the amendments presented in this paper.

Independent claim 51 and dependent claims 60-65, 68-70, 72-75, 78-79, 84, and 115-116 have been cancelled to facilitate prosecution, rendering the rejection of these claims moot. The remaining dependent claims have been amended, as necessary, to depend from claim 1. Because claim 1 has been amended to incorporate the limitations of previously presented claim 93, all claims now recite additional elements that are not taught or suggested by Kawabata and

Janssens. Indeed, the Office has previously acknowledged not rejecting claim 93 (and claims 39 and 42) over Kawabata in view of Janssens. *See* Office Action, March 19, 2009, page 13 (“Kawabata et al does not teach the limitations of 39, 42, and 93 and as such these claims are not rejected in the above 35 USC 103(a) rejection [over Kawabata in view of Janssens].”).

Applicants submit that the remaining pending claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 86, 88-89, 91-92, 95, 101-102, and 105-106 subject to this rejection, which now incorporate the limitations of claim 93, should be allowed for the reasons presented below in Section II.G., in which Applicants address the rejection applied to claim 93.

B. Office Action, Section 8 at page 13: Claims 53 and 55-58

Claims 53 and 55-58 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata in view of Janssens as applied to claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 51, 60-65, 68-70, 72-75, 78-79, 84, 86, 88-89, 91-92, 95, 101-102, 105-106, and 115-116, further in view of Kaniansky. Applicants respectfully traverse these rejections in view of the amendments presented in this paper.

Claims 53 and 55-58 are amended to depend from claim 1, which, as noted, is amended to incorporate the limitations of claim 93. Applicants submit that claims 53 and 55-58, which now incorporate the limitations of claim 93, should be allowed for the reasons presented below in Section II.G., in which Applicants address the rejection applied to claim 93.

C. Office Action, Section 9 at page 15: Claim 66

Claim 66 was rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata in view of Janssens as applied to claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 51, 60-65, 68-70, 72-75, 78-79, 84, 86, 88-89, 91-92, 95, 101-102, 105-106, and 115-

116, further in view of Brown. Applicants respectfully traverse this rejection in view of the amendments presented in this paper.

Claim 66 is amended to depend from claim 1, which, as noted, is amended to incorporate the limitations of claim 93. Applicants submit that claim 66, which now incorporates the limitations of claim 93, should be allowed for the reasons presented below in Section II.G., in which Applicants address the rejection applied to claim 93.

D. Office Action, Section 10 at page 17: Claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, 91-92, 101-112, and 115-118

Claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, 91-92, 101-112, and 115-118 (but not claim 93) were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Chen, in view of Xu and Janssens. Applicants respectfully traverse these rejections in view of the amendments presented in this paper.

Independent claim 51 and dependent claims 60-65, 67-75, 78-79, 84, and 115-118 have been cancelled to facilitate prosecution, rendering the rejection of these claims moot. Dependent claims 3-4, 8-14, 16-27, 29, 31-32, 35, 37-38, 43-44, 86, 88-89, 91-92, and 101-108 have been amended, as necessary, to depend from claim 1. Dependent claims 41 and 109-112 depend from claim 39. Because claims 1 and 39 have been amended to incorporate the limitations of previously presented claim 93, all claims now recite additional elements that are not taught or suggested by Chen, Xu, and Janssens. Indeed, as set forth below, the Office based its rejection of claim 93 on Chen, in view of Xu and Janssens, further in view of Kaniansky, further in view of Brown.

Applicants submit that the remaining pending claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 86, 88-89, 91-92, and 101-112 subject to this rejection, which now incorporate

the limitations of claim 93, should be allowed for the reasons presented below in Section II.G., in which Applicants address the rejection applied to claim 93.

E. Office Action, Section 11 at page 30: Claims 53 and 55-58

Claims 53 and 55-58 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Chen in view of Xu and Janssens as applied to claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, and 91-92 further in view of Kaniansky. Applicants respectfully traverse these rejections in view of the amendments presented in this paper.

Claims 53 and 55-58 are amended to depend from claim 1, which, as noted, is amended to incorporate the limitations of claim 93. Applicants submit that claims 53 and 55-58, which now incorporate the limitations of claim 93, should be allowed for the reasons presented below in Section II.G., in which Applicants address the rejection applied to claim 93.

F. Office Action, Section 12 at page 33: Claim 66

Claim 66 was rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Chen in view of Xu and Janssens as applied to claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, and 91-92, further in view of Brown. Applicants respectfully traverse these rejections in view of the amendments presented in this paper.

Claim 66 is amended to depend from claim 1, which, as noted, is amended to incorporate the limitations of claim 93. Applicants submit that claim 66, which now incorporates the limitations of claim 93, should be allowed for the reasons presented below in Section II.G., in which Applicants address the rejection applied to claim 93.

G. Office Action, Section 13 at page 35: Claims 93 and 119-120

Claims 93 and 119-120 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Chen in view of Xu and Janssens and further in view of Kaniansky as applied to claims 53 and 55-58, further in view of Williams. Applicants respectfully traverse these rejections for the reasons set forth below.

The limitations of claim 93 have been incorporated by amendment into independent claims 1, 39, and 42. Claims 119-120 have been cancelled in favor of claims 101-102, which recite the same limitations.

The Office Action states that, with respect to claim 93, Chen teaches a method of detecting an analyte in a sample that involves contacting a sample containing the analyte with a labeled immunoglobulin. Office Action, page 35. According to Chen, the label may be a BODIPY labeled oligonucleotide and the immunoglobulin may be an antibody, which, the Office Action states, teaches the use of an affinity molecule/charged carrier molecule conjugate. *Id.* at 36. The Office Action also states that Chen teaches forming a complex between the analyte and the immunoglobulin, and then separating complexed from uncomplexed immunoglobulins using a capillary tube with an internal diameter of about 2 μm to about 2000 μm . *Id.* Chen does not teach, however, contacting the analyte with the affinity molecule in the presence of a polyanion, and, as the Office Action acknowledges, Chen also does not teach a separation buffer with polyanions. *Id.*; *see also id.* at 19, 24, 26. Nor does Chen teach concentrating the complex in the presence of a polyanion, or that performing the contacting, concentrating, and separating steps in the presence of a polyanion reduces interference with “noise constituents” (see the subject specification, paras. [0014]-[0016]).

The Office Action presents Xu for the teaching that adding poly(dIdC) to an incubating solution blocks nonspecific binding. *Id.* at 37.

The Office Action next states that Janssens teaches adding a polyanion to a capillary buffer in a capillary electrophoresis detection method. *Id.* That is, Janssens allegedly teaches separating substances in a separation channel in the presence of a third polyanion. (In view of the amendments, the separating step is performed in the presence of the third polyanion.) Janssens teaches, the Office Action states, that “the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated.” *Id.*

The Office Action finds that Kaniansky teaches using isotachophoresis (ITP) as a concentration pretreatment using a capillary electrophoresis chip. *Id.* The Office Action further states that Kaniansky “teaches using a polyanion (methylhydro[xy]ethylcellulose) . . . in the buffer solution for the ITP.” *Id.* at 38. (In view of the amendments, the concentrating step is performed in the presence of the second polyanion.)

The Office Action concludes “[t]herefore the combination of Chen, Xu, Janssens and Kaniansky teaches a solution of the analyte with a first polyanion, separating an analyte using a concentration channel with a second polyanion and then electrophoretically separating the complex and any unbound conjugate using a separation channel and a third polyanion.” *Id.*; *see also id.* at 28-29 (discussing reason for combining Janssens with Chen and Xu), *id.* at 31-32 (discussing reason for combining Kaniansky with Chen, Xu, and Janssens).

But, the Office then acknowledges that the combination of the four references does not teach that the concentration channel has at least one microscale dimension of between about 0.1 and 500 microns. *Id.* The Office finds, however, that Williams teaches that the ITP (i.e., concentration) channel can be 250 microns. Finally, the Office concludes that it would be

obvious to modify “the method of Chen, Xu, Janssens, and [Kaniansky]” to use ITP channels of a size as taught by Williams because it would have been obvious to choose from a finite number of micron lengths of ITP channels with a reasonable expectation of success. *Id.*

Applicants traverse this rejection on several grounds. First, Applicants respectfully submit that, as set forth below in detail, at least two references, Janssens and Kaniansky, do not teach the claimed elements as alleged by the Office. Second, the combination of references presented does not establish a prima facie case of obviousness. The claimed invention as a whole would not have been obvious to one of skill in the art. Applicants respectfully submit that all the claim limitations are not taught or otherwise suggested by the prior art.

First, as to the Janssens reference, the Office Action relies on it for allegedly teaching separating a complex in the presence of a (third) polyanion and thereby reducing interference with separating the complex. According to the Office Action, Janssens teaches “adding a polyanion . . . to a capillary buffer in a capillary electrophoresis detection method,” and that “the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated.” *Id.* at 37; *see also id.* at 26, 28. From this, the Office concluded that the “shorter migration time would reduce the interference between the complex and the capillary column and as a result the polyanion would reduce interference with separating the complex.” *Id.* at 29.

Applicants submit that Janssens does not teach that the third polyanion reduces interference with separating the complex, as recited in claims 1, 39, and 42, and all claims depending therefrom. First, it is not clear why, according to the rationale offered in the Office Action, a shorter migration time would reduce (in relative terms) the degree of interference between an analyte and the capillary column. In any event, Janssens is concerned with stabilizing electroosmotic flow (“EOF”), not with reducing interference with capillary walls per

se. *See* Janssens, col. 2, lines 41-45; col. 7, lines 18-28; col. 16, lines 50-55; col. 19, lines 43-54; col. 21, lines 1-14, 47-49. On the other hand, the claimed invention is primarily concerned with reducing interference from sample constituents, that is, with “noise constituents” which derive from the sample, not interference due to the separation channel’s walls. *See* the subject specification, paras. [0014]-[0016], [0052]. To this end, the claims recite that “the first, second, and third polyanions reduce interference with separating the complex.” *See, e.g.*, claim 1 as currently amended. Janssens neither teaches nor suggests that there even is interference with the assay due to other sample constituents, let alone that a polyanion can block interference with the separation assay “by interacting with sample constituents that interfere with the assay.” *Id.* at [0052].

Note too, that Janssens does not disclose the separation of complexes but only of non-complexed analytes. *See, e.g.*, Janssens, col. 23, lines 21-23; col. 26, lines 64-65; col. 31, lines 35-40, 55-58; col. 32, lines 49-51; col. 33, lines 1-3, 58-62. All of the samples that Janssens uses for illustrating the methods, such as aniline and benzene derivatives and even blood or serum, are analyzed in terms of the separation achieved for each single, uncomplexed component of the sample. The reference by Janssens to ion-pairing between a positively-charged analyte and a polyanion in col. 8, lines 1-6, refers to the interaction between an analyte and the separation medium component, and how that interaction might influence the migration time of single, uncomplexed analyte.

Applicants submit that Janssens does not teach or suggest the separation of complexed analyte species, nor the use of polyanions to reduce interference with separating such analyte(s). *See, e.g.*, claim 1 as currently amended. Accordingly, one of skill in the art would not find the claimed invention obviousness in view of Janssens because Janssens does not teach or suggest

the limitation of reduced interference as alleged in the Office Action. For at least this reason, Applicants respectfully request that the rejection be withdrawn.

The Office Action relies on Kaniansky for allegedly teaching concentrating a complex in the presence of a (second) polyanion and thereby reducing inference with separating the complex. According to the Office Action, Kaniansky teaches “using a polyanion (methylhydro[xy]ethylcellulose) (e.g. a [second] polyanion) in the buffer solution for the ITP.” Office Action at 38. The Office subsequently concluded that Kaniansky teaches concentrating the complex in a concentration channel in the presence of a second polyanion. *Id.* Also, the Office reiterated its position that methylhydroxyethylcellulose (“MHEC”) should be considered to be a polyanion over Applicants’ assertion to the contrary, and points to U.S. Patent Application 2008/0273171 to Huth et al. (“Huth”) for its teaching that “methylhydroxyethylcellulose is a polyanionic component having multiple anionic charges.” *Id.* at 39.

Applicants agree that Huth discloses a polyanionic cellulose compound, but that compound is not MHEC as disclosed by Kaniansky. Huth refers to polyanions such as “metal carboxy methylhydroxyethylcelluloses.” Huth, col. 7, para. [0075], line 10 (emphasis added). As such, the cellulose is carboxylated, and therefore contains anionic carboxylate groups. The cellulose compound would otherwise have no charge.

The structures of MHEC and a metal carboxy methylcellulose can be found in the Sigma-Aldrich Catalog. (Sigma-Aldrich Corp. specializes in organic and inorganic chemicals for chemical synthesis, medicinal chemistry, and materials science. The company markets over 100,000 different chemicals. *See, e.g.*, www.sigmaaldrich.com/customer-service/about-us.html.) A copy of the web site’s catalog pages for methyl 2-hydroxyethyl cellulose (MHEC) and sodium

carboxymethyl cellulose are attached. Also, page 27 of the “Biocompatible/Biodegradable Materials” section of an Aldrich catalog is provided. This page shows both MHEC and a carboxymethyl derivative and the structures of the two types of compounds.

As these catalog entries show, MHEC is a cellulose compound which has side groups attached to the polymer “backbone” that are represented by “OR.” The “OR” groups either represent ethers or hydroxy groups ($R = \text{CH}_3$; or $(\text{CH}_2\text{CH}_2\text{O})_x\text{H}$ or H , respectively. These groups are not anionic. Thus, the MHEC compound disclosed by Kaniansky is not a polyanion.

In contrast, the Sigma-Aldrich catalog entry for sodium carboxymethyl cellulose compound, which corresponds to the metal carboxy methylhydroxyethylcelluloses of the type disclosed by Huth, confirms that this compound is anionic. The structure reveals that in this case, the side chains comprise “OR” groups, but now R may be H or $-\text{CH}_2\text{COO}^-\text{Na}^+$. Thus, the carboxy cellulose derivatives contain side chains that are carboxylates, which makes the compound a polyanion in solution. However, Kaniansky did not disclose or teach the use of carboxylated cellulose derivatives. And, importantly, carboxylated cellulose derivatives as disclosed by Huth would not work for the purpose for which Kaniansky used MHEC.

Specifically, Kaniansky used MHEC to suppress electroosmotic flow. *See* Kaniansky, p. 3598, right column, last line – p. 3599, first paragraph; p. 3599, right column, end of first full paragraph. Kaniansky explains that conducting capillary electrophoresis experiments without EOF (and without hydrodynamic flow), yields the highest reproducibility and reliability of quantitative CE results. *See id.*, p. 3599, right column, first paragraph.

Accordingly, it would be understood by one of skill in the art that Kaniansky did not teach a concentrating step in the presence of a polyanion. Kaniansky taught performing ITP under conditions in which EOF is suppressed, and MHEC, a neutral compound, was either added

to the electrolyte or coated on the walls for the purpose of suppressing EOF. The existence of other cellulose derivatives that happen to be polyanions does not change the fact that Kaniansky did not teach the use of polyanions. The substitution of polyanionic celluloses would not be suggested either, because Kaniansky used MHEC to suppress EOF, whereas a polyanion would generally be regarded as a promoter (albeit an unpredictable one) of EOF, as explained by Janssens. *See* Janssens, col. 19, lines 3-12.

Applicants submit that Kaniansky does not teach or suggest the concentration of analytes in the presence of a polyanion, nor, therefore, could the reference teach or suggest the use of polyanions to reduce interference with separating the analyte(s). Accordingly, one of skill in the art would not find the claimed invention obviousness in view of Kaniansky because Kaniansky does not teach or suggest the limitation of a second polyanion or reduced interference as alleged in the Office Action. For at least this reason, Applicants respectfully request that the rejection be withdrawn.

Applicants also respectfully submit that the combination of references presented does not establish a prima facie case of obviousness. Viewing the references as a whole, one of skill in the art would not combine the references and arrive at the claimed invention.

Even assuming, without acquiescing to the presumption that Chen in view of Xu suggests contacting a sample with an affinity molecule/charged carrier conjugate in the presence of a first polyanion, there is no rational underpinning to support combining this suggestion with the teachings of Janssens or Kaniansky. The teachings of Janssens and Kaniansky are at odds with one another and would lead one of skill in the art away from combining them with each other. Furthermore, even combining the teachings of Janssens and/or Kaniansky with Chen and Xu would not suggest the claimed invention.

Janssens teaches that the addition of both a polycation and a polyanion result in a stable and more reproducible EOF, and that the addition of both charged polymers is necessary. Janssens, col. 18, lines 15-22; col. 19, lines 3-16; col. 21, lines 1-7 (note that the “initiator of Janssens is a polymer with positive charges, *see* col. 10, lines 45-54). In contrast, Kaniansky teaches the use of a neutral polymer for suppressing EOF. Kaniansky, p. 3599, right column, last sentence of first full paragraph. The motives provided by Janssens and Kaniansky are contradictory, as one seeks to stabilize EOF while the other teaches the need to suppress EOF. It is well-established that the proposed modification cannot render the prior art unsuited for its intended purpose, or that it cannot change the principle of operation of a reference. *See* MPEP § 2143.01.V-VI. Here, an attempt to combine Janssens and Kaniansky would do just that because their teachings are mutually exclusive.

Note too that neither Janssens nor Kaniansky teaches or suggests adding a second or third polyanion in order to reduce interference with separating the analyte(s) due to “noise constituents” in a sample. The teachings of these references primarily concern methods for achieving stable and reproducible migration times in capillary electrophoresis experiments through the control of EOF (albeit using contradictory means for contradictory purposes), with no suggestion that materials (polyanions in particular) should be added in order to interact with sample noise constituents that would otherwise interfere with the assay. *See* subject specification, para. [0052]. Nor do Chen and Xu teach or suggest a separation or concentration step performed in the presence of a second or third polyanion. Williams also does not teach or suggest a second or third polyanion. Thus, there is simply no suggestion found in the prior art references for using polyanions to reduce interference as in the claimed invention. The prior art

references cannot support a prima facie case of obviousness as no rationale exists for combining these reference to achieve the claimed invention.

For the reasons stated above, Applicants respectfully request that the rejection applied to claim 93, the limitations of which are now incorporated into all pending claims, over Chen in view of Xu and Janssens, further in view of Kaniansky, and further in view of Williams under § 103, be withdrawn, thereby placing all pending claims as amended herein in condition for allowance.

H. Office Action, Section 14 at page 40: Claims 95-96 and 98-99

Claims 95-96 and 98-99 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Chen in view of Xu and Janssens as applied to claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, and 91-92, further in view of Kawabata. Applicants respectfully traverse these rejections in view of the amendments presented in this paper.

Claims 95-96 depend from claim 1 and claims 98-99 depend from claim 39, which, as noted, are both amended to incorporate the limitations of claim 93. Applicants submit that claims 95-96 and 98-99, which now incorporate the limitations of claim 93, should be allowed for the reasons presented above in Section II.G., in which Applicants address the rejection applied to claim 93.

I. Office Action, Section 15 at page 42: Claims 42 and 113-114

Claims 42 and 113-114 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Hosokawa et al. (“Hosokawa”) in view of Xu and Janssens. Applicants respectfully traverse these rejections in view of the amendments presented in this paper.

Claims 113-114 depend from claim 42, which, as noted, is amended to incorporate the limitations of claim 93. Applicants submit that claims 42 and 113-114, which now incorporate the limitations of claim 93, should be allowed for the reasons presented above in Section II.G., in which Applicants address the rejection applied to claim 93.

J. Office Action, Section 16 at page 46: Claim 100

Claim 100 was rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Hosokawa, in view of Xu and Janssens as applied to claims 42 and 113-114, and further in view of Kawabata. Applicants respectfully traverse these rejections in view of the amendments presented in this paper.

Claim 100 depends from claim 42, which, as noted, is amended to incorporate the limitations of claim 93. Applicants submit that claim 100, which now incorporate the limitations of claim 93, should be allowed for the reasons presented above in Section II.G., in which Applicants address the rejection applied to claim 93.

III. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully requests that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 53, 55-58, 66, 86, 88-89, 91-92, 95-96, and 98-114 in condition for allowance. Applicants submit that the proposed amendments of claims 1, 3-4, 8, 31-32, 37-39, 41-42, 53, 55-58, 66, 86, 88-89, and 91-92 do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Furthermore, Applicants respectfully point out that the final action by the Examiner presented some new arguments as to the application of the art against Applicants' invention. It is respectfully submitted that the entering of the Amendment would allow the Applicants to reply to the final rejections and place the application in condition for allowance.

Finally, Applicants submit that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.


In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicants therefore requests the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

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By: 
David Albagli
Reg. No. 56,155
(650) 849-6600
E-mail: david.albagli@finnegan.com

Attachments: Sigma-Aldrich Catalog, Methyl 2-hydroxyethyl cellulose
Sigma-Aldrich Catalog, Sodium carboxymethyl cellulose
Aldrich Catalog, Biocompatible/Biodegradable Polymers, p. 27